

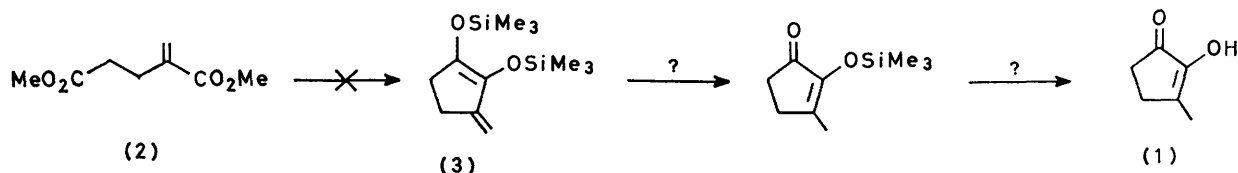
## Synthesis of 2-Hydroxy-3-methylcyclopent-2-en-1-one from Methyl Acrylate†

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The title compound was prepared in 55% yield from the dimer of methyl acrylate, dimethyl 2-methylenepentane-dioate. The crucial step in the synthesis involved silica gel as a reaction medium.

2-HYDROXY-3-METHYLCYCLOPENT-2-EN-1-ONE ('corylone,' 'cyclotene,' 'nussol,' *etc.*) (1) is a commercially important perfumery and flavouring material possessing a sweet and very powerful spicy-coffee-caramel odour. Although in recent years many syntheses of this and similar structures have been published,<sup>1</sup> the majority suffer from low yields, multistep procedures, and/or expensive reagents. We now describe a simple synthesis of this compound in high yield in three steps from the

unsaturation contained in the molecule, since treatment of the reduced diester (4) under similar conditions gave the corresponding bis(trimethylsilyl) ether (5) in >90% yield. In order to overcome this problem, therefore, it was found necessary to protect the double bond before acyloin condensation. The dimethylamine adduct (6)<sup>4</sup> [formed in almost quantitative yield from (2) and methanolic dimethylamine] was smoothly reduced by sodium in boiling toluene to (7) in 78% yield.



dimer of methyl acrylate, dimethyl 2-methylenepentane-dioate (2).

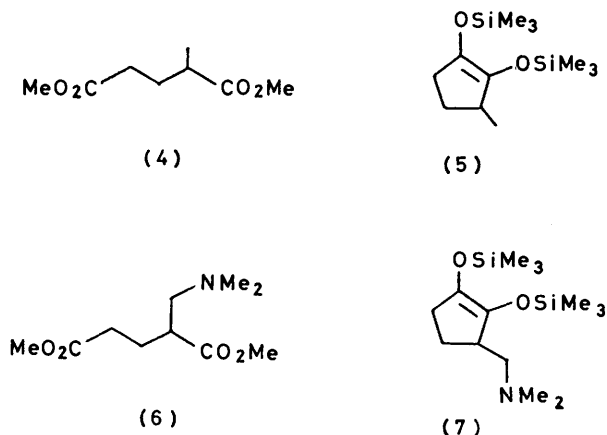
Our initial intent was to cyclise the diester by the acyloin reaction to give the bis(trimethylsilyl) ether (3). Simple hydrolysis of this ether would then give (1) directly. Treatment of methyl acrylate with tris-(cyclohexyl)phosphine in pyridine<sup>2</sup> gave the required

Although it had been envisaged that simple hydrolysis and quaternisation of such a species would lead to (1) directly (see Scheme 1), a novel procedure utilising silica gel as a reaction medium proved the most efficient of the many methods tried for the transformation. Thus elution of (7) down a silica column produced pure (1) in 70% yield.

This method not only constitutes a highly efficient synthesis of corylone in 55% yield from the acrylate dimer (2) (or 43% from methyl acrylate itself) but also has the additional advantage that the desired product is the only one eluted. (No trace of dimethylamine or siloxane was observed.) The chromatography support thus acts not only as a reaction medium but also in the normal way as a purification system.

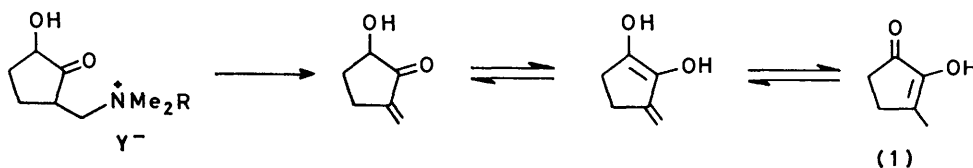
### EXPERIMENTAL

M.p.s were determined with a Köfler hot-stage apparatus. Proton n.m.r. spectra were recorded at 60 MHz on a Perkin-Elmer R12 spectrometer and at 100 MHz on a Varian HA-100 or XL-100/12 spectrometer with tetramethylsilane as an internal standard. I.r. spectra were recorded on a Perkin-Elmer 157G spectrophotometer. Mass spectra were recorded, unless otherwise noted, at 70 eV on an A.E.I. MS12 spectrometer, either by direct ionisation, or through a g.l.c. inlet system. Major ion fragments are quoted as percentages of the base peak (100%), which were measured with a Digispec model PDP8 data system.



dimer in good yield. To our surprise, however, (2) proved to be inert under all the normal conditions used for the acyloin reaction.<sup>3</sup>

We suspected the source of our problem to lie in the



SCHEME 1

† No reprints available.

Column chromatography was carried out with 100–200 mesh silica gel (B.D.H.).

Petroleum refers to the fraction of b.p. 40–60 °C which was distilled before use. Ether, where described as dry, was of reagent grade quality and stored over clean sodium wire. Pyridine was stored over potassium hydroxide pellets and distilled immediately before use. Toluene was distilled; the first 10 and last 15% were discarded. The distillate was refluxed for 24 h over sodium, under nitrogen, before it was distilled (under nitrogen) for use.

**Dimethyl 2-Methylenepentanedioate (2).**—Methyl acrylate (30.0 g, 349 mmol) (distilled immediately before use) and dry pyridine (30 ml) containing tris(cyclohexyl)phosphine-carbon disulphide complex<sup>5</sup> (2.0 g, 6 mmol) were refluxed under nitrogen for 16 h. The deep red solution was cooled and the pyridine removed under reduced pressure. The residue was taken up in diethyl ether (400 ml) and the solution washed with aqueous 1M-hydrochloric acid (3 × 40 ml). The combined aqueous layers were extracted with ether (2 × 50 ml) and the combined organic layers washed with 1M-hydrochloric acid (30 ml), saturated brine (40 ml), and saturated aqueous sodium hydrogen carbonate (2 × 30 ml), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. Distillation of the oil obtained gave dimethyl 2-methylenepentanedioate (2) (23.8 g, 79%) as a liquid, b.p. 66–68 °C at 1 mmHg (lit.,<sup>2b</sup> 110 °C at 14 mmHg),  $\nu_{\max}$  (film) 1 738, 1 715, and 1 635 cm<sup>-1</sup>,  $\tau$ (CDCl<sub>3</sub>) 3.77 (1 H, br), 4.37 (1 H, br), 6.22 (3 H, s), and 6.31 (3 H, s), *m/e* 172 (*M*<sup>+</sup>, 1%), 141 (48), 140 (74), and 112 (100).

**Dimethyl 2-(Dimethylaminomethyl)pentanedioate (6).**—To a stirred solution of dimethylamine (28%) in anhydrous methanol (100 ml) held at 0 °C (ice-bath), under nitrogen, was added, *via* a syringe, dimethyl 2-methylenepentanedioate (2) (10.3 g, 60 mmol) in one portion. The solution was stirred for 4 h, during which period the temperature never exceeded 5 °C. Removal of the excess of amine and methanol under reduced pressure gave a pale yellow oil, which was distilled at reduced pressure to give dimethyl 2-(dimethylaminomethyl)pentanedioate (6) (12.8 g, 99%) as an oil, b.p. 81–83 °C at 0.4 mmHg,  $\nu_{\max}$  (film) 1 735 cm<sup>-1</sup>,  $\tau$ (CDCl<sub>3</sub>) 6.31 (3 H, s), 6.33 (3 H, s), 7.78 (6 H, s), and 7.0–8.2 (7 H, m), *m/e* (15 eV) 217 (*M*<sup>+</sup>, 3%), 59 (4), and 58 (100).

**3-(Dimethylaminomethyl)-1,2-bis(trimethylsilyloxy)cyclopentene (7).**—To a 500 ml, three-necked flask containing a 'football' stirrer, equipped with a reflux condenser and a 100 ml pressure-equalising dropping funnel (maintained under oxygen-free nitrogen), were added toluene (200 ml) and sodium (4.0 g, 174 mmol). The toluene was brought to reflux on an oil-bath (bath temp. 135 °C) and the mixture stirred until a fine dispersion of sodium had been produced.

Dimethyl 2-(dimethylaminomethyl)pentanedioate (6) (10.4 g, 48 mmol) and chloro(trimethyl)silane (20.0 g, 184 mmol) (distilled from calcium hydride, under nitrogen, immediately prior to use) in dry toluene (80 ml) were added dropwise over 2 h. A dark purple precipitate appeared within a few minutes of the ester's being added. After heating and stirring for a further 12 h, the contents of the flask were cooled and filtered, under nitrogen, through a three-inch number three sinter. The precipitate was washed with anhydrous petroleum (3 × 40 ml). The solvent was removed under reduced pressure to give a pale yellow oil that was purified by short-path distillation (bath temp. 85 °C at 0.1 mmHg) to give the *bis-silyl ether* (7) (11.2 g, 78%), *M*<sup>+</sup> 301.189 5 (C<sub>14</sub>H<sub>31</sub>NO<sub>2</sub>Si<sub>2</sub> requires *M*, 301.189 3),  $\nu_{\max}$  (CCl<sub>4</sub>) 1 700 cm<sup>-1</sup>,  $\tau$ (CDCl<sub>3</sub>) 7.20–8.38 (7 H, m), 7.83 (6 H, s), and 9.86 (18 H, s), *m/e* 301 (*M*<sup>+</sup>, 3%), 243 (26), 169 (49), 147 (59), 58 (100), and 45 (33).

**2-Hydroxy-3-methylcyclopent-2-enone (1).**—The bis-silyl ether (7) (1.0 g, 3 mmol) was dissolved in anhydrous ether (50 ml) under nitrogen. The solution was added to a column of silica gel (150 g) (made in 2 : 1 petroleum–diethyl ether) over 15 min. The material was eluted with petroleum–diethyl ether (2 : 1; 200 ml). Elution was halted for 6 h; further elution after that (1 : 1 petroleum–diethyl ether) gave the ketone (1) (0.26 g, 70%),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3 500, 1 710, and 1 605 cm<sup>-1</sup>,  $\tau$ (CDCl<sub>3</sub>) 3.21 (1 H, br, s, removed by D<sub>2</sub>O), 7.59 (4 H, s), and 8.00 (3 H, s), *m/e* 112 (*M*<sup>+</sup>, 100%), 83 (22), 69 (44), 55 (26), 43 (27), and 41 (39). The spectroscopic properties were identical with those of an authentic sample.

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